Ketamine Cystitis: A Case Report
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Abstract
Ketamine misuse is the most common illicit drug used in Singapore, Hong Kong and areas of China and Taiwan. A Chinese American male presented to our inpatient rehabilitation unit with genital urinary complaints, of hematuria, dysuria and frequency. He had been misusing ketamine for many years and had similar complaints in the past. Healthcare providers should be aware that ketamine user disorder may present primarily with genital urinary complaints. Cessation of ketamine use is of utmost importance since chronic irreversible fibrosis of the genital urinary tract may occur with continued misuse.

Introduction
Ketamine hydrochloride, a noncompetitive N-Methyl-D-Aspartate (NMDA) receptor antagonist, was initially introduced in the 1960’s as a dissociative anesthetic [1]. Ketamine noncompetitively binds to the PCP receptor and inhibits glutamate activation of the NMDA channel [2]. In recent years it has been studied for its rapid antidepressant effects, particularly with treatment-resistant depression patients.

In addition, ketamine has been frequently used recreationally since the 1980’s, particularly in the nightlife and club environment [2]. Also known by its street name “Special K,” the drug can be sniffed, smoked, taken PO, or injected. Users of the drug experience decreased inhibitions and a dissociative mental state [2]. At high doses, users experience nausea, increased heart rate and blood pressure, and potentially a cataleptic-like, "out-of-body" or "near-death" experience, which is referred to among users as a "K-hole" [3].

Ketamine use has increased dramatically in the last decade, reaching a worldwide prevalence of 5.7 percent of all drug users [4]. Pal et al. (2013) found that 18.7 percent of drug users in the United States have reported lifetime use of ketamine [5], and 5.8 percent had used it recently. Misuse of ketamine is particularly widespread in Southeast Asian countries, and it is the single most abused illicit drug in Hong Kong [6].

Habitual ketamine use is also associated with genitourinary symptoms, such as dysuria, debilitating urinary frequency, urgency, urge incontinence and hematuria [7]. One of the most commonly associated symptoms is ulcerative cystitis [1,8,9]. The incidence of lower urinary tract symptoms in ketamine misusing patients is approximately 30 percent, and in general, affected patients tend to be young with a peak age range of 16 to 35 years [10]. Ketamine-induced cystitis was only first identified in 2007 [1], and the pathophysiology has yet to be completely elucidated [9].

Case Report
A 24 year-old Chinese-American heterosexual male was admitted to an inpatient addiction rehabilitation program for the treatment of intranasal ketamine use disorder. The patient’s mother died when he was 21 years old, and he lives at home with his father and sister. He has smoked a pack of cigarettes per day since age 17. His psychiatric history is unremarkable.

The patient reported daily intranasal ketamine use beginning at age 20. He has since had several failed attempts of abstinence. His drug use is strictly limited to ketamine, and he has not combined ketamine with any other illicit or prescribed controlled prescription medications. On admission, the patient reported several urinary complaints, which included frequency, urgency, dysuria, gross hematuria, and suprapubic pain. His physical examination was within normal limits, with the exception of moderate suprapubic pain on palpation. There were no genital lesions, no inguinal adenopathy, and no penile discharge. His medical history is otherwise negative.

On laboratory examination, the complete blood count and comprehensive metabolic profile were within normal limits. Routine urinalysis revealed gross hematuria, with a red blood cell of >182 per high power field, and a white blood cell count of 96 per high power field. Chlamydia trachomatis and gonococcal DNA, SDA test, syphilis serology, and HIV antibody were all negative. Urine immunoassay toxicology was negative for opiates, cocaine, methadone, amphetamine, THC, and benzodiazepines. Urine drug toxicology was not performed for ketamine.
The patient was treated symptomatically with NSAIDS and acetaminophen. Oxybutynin, an anticholinergic antispasmodic at 5 mg PO TID was added to the regimen. His urinary signs and symptoms gradually improved during his three-week admission. He was advised to remain totally abstinent from ketamine, and informed that continued use would lead to increasing urinary tract complications.

Discussion

This patient presented clinically with typical signs and symptoms of ketamine-associated cystitis. The patient was a long-term regular user of ketamine and had the classic signs and symptoms of urinary tract complications.

Ketamine-associated cystitis was first identified in 2007 [1]. The incidence of lower urinary tract symptoms in ketamine misusing patients is approximately 30 percent [10]. Males and females are equally affected [8].

Studies have suggested that chronic ketamine use may induce an autoimmune or inflammatory response in the bladder wall [8,9], neovascularization and petechial hemorrhage [7], as well as complications involving ureteral wall thickening, and irregular bladder mucosa and hydronephrosis [11,12]. A recent study showed that ketamine-induced ulcerative cystitis and bladder apoptosis involves oxidative stress mediated by mitochondria and the endoplasmic reticulum [13].

Failure to recognize and delayed diagnosis of ketamine-induced cystitis may result in irreversible renal tract damage, requiring surgical intervention [12], and/or resulting in renal failure requiring dialysis [8]. Urinary tract protective agents such as chondroitin sulfate, pentosanpolysulfate, and hyaluronic acid have been shown to result in some short-term benefit [8,10]. Complete and timely abstinence from ketamine is the most effective strategy for preventing ongoing ketamine cystitis and urinary tract damage [14].

References